

CLAIMS:

- 1 A method of making 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole, which method comprises the steps in sequence of: (i) reacting bromine with a solution of 4-acetamido-cyclohexanone in water to produce 2-bromo-4-acetamido-cyclohexanone; (ii) adding thiourea to produce 6-acetylamino-2-amino-4,5,6,7-tetrahydro-benzthiazole; (iii) adding an aqueous solution of hydrobromic acid to produce 2,6-diamino-4,5,6,7-tetrahydro-benzthiazole; and (iv) isolating 2,6-diamino-4,5,6,7-tetrahydro-benzthiazole.
- 2 A method according to claim 1 wherein step (iii) is carried out without isolating the 6-acetylamino-2-amino-4,5,6,7-tetrahydro-benzthiazole produced in step (ii).
- 3 A method according to claim 1 or 2, wherein any three successive steps of steps (i) to (iv) are carried out in a single reaction vessel.
- 4 A method according to claim 1, 2 or 3, wherein steps (i) to (iv) are carried out in a single reaction vessel.
- 5 A method according to claim 1, 2, 3 or 4, further comprising, prior to step (i), the step of oxidising 4-acetamido-cyclohexanol to produce 4-acetamido-cyclohexanone.
- 6 A method according to claim 5, wherein the step of oxidising 4-acetamido-cyclohexanol to produce 4-acetamido-cyclohexanone and at least three successive steps of steps (i) to (iv) are carried out in a single reaction vessel.
- 7 A method according to any preceding claim wherein in step (i) the solution of 4-acetamido-cyclohexanone in water and bromine are combined at a temperature of from 15°C to 40°C.

8 A method according to any preceding claim wherein, after the bromine and the 4-acetamido-cyclohexanone solution have been combined, the mixture is heated to a temperature of from 40°C to 50°C, and maintained at or near this temperature until the bromination is complete.

9 A method according to any preceding claim wherein, in step (ii), the temperature is increased to 70°C to 90°C.

10 A method according to any preceding claim, wherein step (iii) is carried out under refluxing conditions.

11 A method according to any preceding claim wherein, after step (iii) but before step (iv), the reaction mixture is cooled to 5°C to 20°C, then neutralised.

12 A method according to any preceding claim, further comprising the step of resolving the 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole isolated in step (iv) into its R(+) and S(-) enantiomers and recovering the R(+) and/or S(-) enantiomer.

13 A method of synthesising pramipexole, comprising the steps of : forming 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole by a method according to any preceding claim, and converting it to pramipexole.

14 A method according to claim 13, wherein 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole is converted to pramipexole by reaction with a propionyl halide.

15 A method according to claim 13 or 14, wherein the 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole comprises the R(+) enantiomer.

- 16 A method according to claim 13 or 14, wherein the 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole comprises the S(-) enantiomer.
- 17 A method according to claim 13 or 14, wherein the 2,6-diamino-4,5,6,7-tetrahydro-benzothiazole comprises a racemic mixture.
- 18 A method according to claim 14, further comprising the step of resolving the pramipexole into its R(+) and S(-) enantiomers and recovering the R(+) and/or S(-) enantiomer.
- 19 A method of synthesizing 2,6-diamino-4,5,6,7-tetrahydro-benzthiazole substantially as herein described with reference to the Examples.